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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,815	06/26/2006	Alan G. Saltzman	USAV2003-0020 US PCT	1806

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
08/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/596,815	SALTZMAN ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 9-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/15/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 4-9-08. Claims 1-4 and 9-10 are pending. Claims 1 and 9 have been amended. Claims 5-8 have been cancelled.

Information Disclosure Statement

2. The information disclosure statement filed 1/15/2008 has been considered. An initialed copy is enclosed.

Objections/Rejections Withdrawn

3. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Rejection of claims 1-2, and 9-10 under 35 U.S.C. 102(a) is withdrawn in light of applicant's amendment thereto.

b) Rejection of 1-2 and 9 under 35 U.S.C. 102(a) is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The rejection of claims 1-4 and 9-10 under 35 U.S.C. 103(a) as being unpatentable over Wisotzkey et al US Application NO. 20030159168 A1 August 21, 2003 in view of Copland et al 2003 (February 14, 2003), Vol. 21 pgs. 883-890.

Applicant arguments:

The Examiner asserts that Copland et al. teach immature dendritic cells uptake antigen and express cell surface markers following incubation with FITC-conjugated antigen, enhanced cell surface marker expression after exposure to FITC-ovalbumin and after exposure to tetanus toxin-stimulated T cells. The Examiner contends that it would have been prima facie obvious at the time the instant invention was made to incorporate measuring autologous T-cell response to tetanus toxin in view of Wisotzkey et al. teaching a method of identifying a compound capable of modulating Cathepsin Z activity in a cell. Claim 1 has been amended to obviate this rejection. The references of Wisotzkey et al. and Copland et al. in combination do not teach or suggest a method of identifying a compound capable of modulating the activity of Cathepsin Z activity in an antigen-presenting dendritic cell. Thus, claim 1 and claims 2-4 and 9- 10 which are ultimately dependent from claim 1, are non-obvious and patentable over the prior art.

Examiner's Response to Applicant's Arguments:

Examiner accepts applicant's amendments thereto and argument. However they are not deemed persuasive. The claims are drawn to a method of identifying a compound capable of modulating the activity of Cathepsin Z in an antigen-presenting dendritic cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin Z activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin Z activity in the presence of said candidate compound. Examiner disagrees that the references of Wisotzkey et al.

and Copland et al. in combination do not teach or suggest a method of identifying a compound capable of modulating the activity of Cathepsin Z activity in an antigen-presenting dendritic cell. Wisotzkey et al teach a method of identifying a compound capable of modulating the activity of Cathepsin Z in a cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin Z activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin Z activity in the presence of said candidate compound (abstract, [0020], [0024]), wherein said cell's level of Cathepsin Z activity is measured by measuring antigen presentation (i.e. macrophages see example 19 and example 20). Therefore Wisotzkey et al anticipate a method wherein cell is an antigen-presenting cell. Wisotzkey et al teach a method for treating an autoimmune disease comprising the step of administering the pharmaceutical of a compound capable of modulating the activity of Cathepsin Z, wherein said autoimmune disease is rheumatoid arthritis (see [0015], [0087], [0089], [0172]. Copland et al teach that dendritic cells are highly potent profession antigen-presenting cells essential for initiation of an immune response. Copland et al teach that immature human dendritic cells were generated from peripheral blood monocytes cultured with GM-CSF and IL-4 and that the uptake of antigen by dendritic cells and the degree of expression of the cell surface markers MHC class II, CD80, CD86 and the DC maturation marker CD83, were investigated by incubation solution containing FITC-conjugated antigen. Copland et al teach that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution. Therefore one would have been motivated to incorporate measuring autologous T-cell response to tetanus toxin, measuring by said cell's capacity to present quenched FITC-ovalbumin, and said antigen-presenting cell such as immature dendritic cell as taught by Copland et al because Copland et al teach that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing

tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution. The limitations have been.

As outlined previously, the claims are drawn to a method of identifying a compound capable of modulating the activity of Cathepsin Z in an antigen-presenting dendritic cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin Z activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin Z activity in the presence of said candidate compound.

Wisotzkey et al is relied upon as set forth supra. However Wisotzkey et al does not teach a method wherein said cell's level of antigen presentation is measured by measuring autologous T-cell response to tetanus toxin, wherein said cell's level of antigen presentation is measured by measuring said cell's capacity to present quenched FITC-ovalbumin, wherein said antigen-presenting cell is selected from the group consisting of dendritic cell precursor, immature dendritic cell, and mature dendritic cell.

Copland et al that dendritic cells are highly potent profession antigen-presenting cells essential for initiation of an immune response. Copland et al teach that immature human dendritic cells were generated from peripheral blood monocytes cultured with GM-CSF and IL-4 and that the uptake of antigen by dendritic cells and the degree of expression of the cell surface markers MHC class II, CD80, CD86 and the DC maturation marker CD83, were investigated by incubation solution containing FITC-conjugated antigen. Copland et al teach that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution.

It would have been prima facie obvious at the time the invention was made to incorporate measuring autologous T-cell response to tetanus toxin, measuring by said cell's capacity to present quenched FITC-ovalbumin, and said antigen-presenting cell such as immature dendritic cell as taught by Copland et al because Copland et al teach

that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution.

5. The rejection of claims 1-4 and and 9-10 under 35 USC §103(a) as allegedly being unpatentable over Thurmond et al WO 2002/21129 in view of Copland et al 2003 (February 14, 2003), Vol. 21 pgs. 883-890 and Wisotzkey et al US Application NO. 20030159168 A1 August 21, 2003 are maintained for the reasons set forth in the previous office action.

Applicant arguments:

The Examiner asserts that Thurmond et al. teaches a method of identifying a compound capable of modulating the activity of Cathepsin S in a cell. The Examiner contends it would have been prima facie obvious at the time the invention was made to incorporate Cathepsin Z as taught by Wisotzkey et al. to the method of Thurmond et al. and incorporate measuring autologous T-cell response to tetanus toxin and measuring the cells capacity to present quenched FITC ovalbumen as taught by Copland et al. The amendment to claim 1 such that claim 1 recites "an antigen-presenting cell" obviates this rejection rendering claim I and dependent claims 2-6, 5 and 9-10 non-obvious and patentable.

Examiner's Response to Applicant's Arguments:

Examiner accepts applicant's amendments thereto and argument. However they are not deemed persuasive. The claims are drawn to a method of identifying a compound capable of modulating the activity of Cathepsin Z in an antigen-presenting dendritic cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin Z activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin Z activity in the presence of said candidate compound. Although Thurmond et al teach a method of identifying a compound capable of modulating the activity of Cathepsin S in a cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin S activity in the absence of a

candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin S activity in the presence of said candidate compound. One would have been motivated at the time modify the method of identifying a compound capable of modulating the activity of Cathepsin as taught by Thurmon et al and substitute Cathepsin S for Cathepsin Z because both teach a method of identifying a compound capable of modulating the activity of Cathepsin.

Furthermore as stated in the previous office action, Copland et al that dendritic cells are highly potent profession antigen-presenting cells essential for initiation of an immune response. Copland et al teach that immature human dendritic cells were generated from peripheral blood monocytes cultured with GM-CSF and IL-4 and that the uptake of antigen by dendritic cells and the degree of expression of the cell surface markers MHC class II, CD80, CD86 and the DC maturation marker CD83, were investigated by incubation solution containing FITC-conjugated antigen. Copland et al teach that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution. Wisotzkey et al teach a method of identifying a compound capable of modulating the activity of Cathepsin Z in a cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin Z activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin Z activity in the presence of said candidate compound (abstract, [0020], [0024]), wherein said cell's level of Cathepsin Z activity is measured by measuring antigen presentation (i.e. macrophages see example 19 and example 20).

Therefore one would have been motivated to incorporate a Cathepsin Z as taught by Wisotzkey et al and modify the method of identifying a compound capable of modulating the activity of Cathepsin as taught by Thurmon et al because both teach a method of identifying a compound capable of modulating the activity of Cathepsin. Therefore one would have been motivated to at the time the invention was made to incorporate measuring autologous T-cell response to tetanus toxin, measuring by said

cell's capacity to present quenched FITC-ovalbumin, and said antigen-presenting cell such as immature dendritic cell as taught by Copland et al into the method as taught by Thurmond et al because Copland et al teach that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution.

As outlined previously, the claims are drawn to a method of identifying a compound capable of modulating the activity of Cathepsin Z in an antigen-presenting dendritic cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin Z activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin Z activity in the presence of said candidate compound.

Thurmond et al teach a method of identifying a compound capable of modulating the activity of Cathepsin S in a cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin S activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin S activity in the presence of said candidate compound.

Copland et al that dendritic cells are highly potent profession antigen-presenting cells essential for initiation of an immune response. Copland et al teach that immature human dendritic cells were generated from peripheral blood monocytes cultured with GM-CSF and IL-4 and that the uptake of antigen by dendritic cells and the degree of expression of the cell surface markers MHC class II, CD80, CD86 and the DC maturation marker CD83, were investigated by incubation solution containing FITC-conjugated antigen. Copland et al teach that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution.

Wisotzkey et al teach a method of identifying a compound capable of modulating the activity of Cathepsin Z in a cell, comprising the steps of: (a) measuring said cell's base level of Cathepsin Z activity in the absence of a candidate compound; (b) introducing said candidate compound; and (c) measuring said cell's level of Cathepsin Z activity in the presence of said candidate compound (abstract, [0020], [0024]), wherein said cell's level of Cathepsin Z activity is measured by measuring antigen presentation (i.e. macrophages see example 19 and example 20). Therefore Wisotzkey et al anticipate a method wherein cell is an antigen-presenting cell. Wisotzkey et al teach a method for treating an autoimmune disease comprising the step of administering the pharmaceutical of a compound capable of modulating the activity of Cathepsin Z, wherein said autoimmune disease is rheumatoid arthritis (see [0015], [0087], [0089], [0172].

It would have been prima facie obvious at the time the invention was made to incorporate a Cathepsin Z as taught by Wisotzkey et al and modify the method of identifying a compound capable of modulating the activity of Cathepsin as taught by Thurmon et al because both teach a method of identifying a compound capable of modulating the activity of Cathepsin. It would also have been prima facie obvious at the time the invention was made to incorporate measuring autologous T-cell response to tetanus toxin, measuring by said cell's capacity to present quenched FITC-ovalbumin, and said antigen-presenting cell such as immature dendritic cell as taught by Copland et al into the method as taught by Thurmond et al because Copland et al teach that exposure to FITC–ovalbumin resulted in enhanced expression of cell surface markers when compared to exposure to antigen in solution. Copland et al teach that expression was highest following exposure to containing tetanus toxoid (TT) stimulated primed T cell proliferation more effectively than TT-neutral liposomes or TT-solution.

New Grounds of Rejection
Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 9-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method for treating an autoimmune disease comprising the steps of administering a pharmaceutical comprising the compound capable of modulating the activity of Cathepsin in the antigen-presenting dendritic cell identified by the method. The specification does not provide any definition or guidance as to the structural, physical or chemical characteristics of a compound. The specification only discloses functionality of a compound, as “capable of modulating Cathepsin Z activity in a cell” (see specification page 11 example 8).

The genus of any compound is vast and encompasses many different proteins and fragments of proteins, etc. with potentially having different functions and which are unrelated by structure and the disclosure fails to adequately define the common structural attributes of the genus of a compound that have the related function. Mere function does not describe a structure, because the specification does not provide relevant identifying characteristics, including a known disclosed correlation between function and structure. The courts have held that in these instances, the specification lacks written description see Enzo Biochem Inc. v. Gen-Probe Inc. 63 USPQD2D 1609 (CAFC 2002) and University of Rochester v. G. D. Searle & Co. 69 USPQ2D 1886 (CAFC 2004). When the genus is vast and compounds (in this case - MPEP § 2163.02

states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc.'v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104).

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Thus the claims do not meet the written description requirement. ***Conclusion***

Deleted: ¶

Status of the Claims

7. Claims 1-4 and 9-10 are rejected.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nina A Archie/
Examiner, Art Unit 1645/N. A. A./

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